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Cancer incidence risks above and below 1 Gy for radiation protection in space

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ABSTRACT

The risk assessment quantities called lifetime attributable risk (LAR) and risk of exposure-induced cancer (REIC) are used to calculate the cumulative cancer incidence risks for astronauts, attributable to radiation exposure accumulated during long term lunar and Mars missions. These risk quantities are based on the most recently published epidemiological data on the Life Span Study (LSS) of Japanese A-bomb survivors, who were exposed to γ-rays and neutrons. In order to analyze the impact of a different neutron RBE on the risk quantities, a model for the neutron relative biological effectiveness (RBE) relative to gammas in the LSS is developed based on an older dataset with less follow-up time. Since both risk quantities are based on uncertain quantities, such as survival curves, and REIC includes deterministic radiation induced non-cancer mortality risks, modelled with data based on the general population, the risks for astronauts may not be optimally estimated. The suitability of these risk assessment measures for the use of cancer risk calculation for astronauts is discussed. The work presented here shows that the use of a higher neutron RBE than the value of 10, traditionally used in the LSS risk models, can reduce the risks up to almost 50%. Additionally, including an excess absolute risk (EAR) baseline scaling also increases the risks by between 0.4% and 8.1% for the space missions considered in this study. Using just an EAR model instead of an equally weighted EAR and excess relative risk (ERR) model can decrease the cumulative risks for the considered missions by between 0.4% and 4.1% if no EAR baseline scaling is applied. If EAR baseline scaling is included, the calculated risks with the EAR- and the mixed model, as well as the risks calculated with just the ERR model are almost identical and only small differences in the uncertainties are visible.

1. Introduction

A good understanding of radiation related detrimental health effects and risk levels is important when planning manned missions into space for either routine or exploratory purposes. Currently different national space agencies set individual limits on either risks or radiation doses, such that mission radiation related risks remain within a predefined acceptable range. A major limiting factor for long-term manned missions is space radiation from galactic cosmic rays (GCR) and from solar particle events (SPE). The GCR can originate outside the solar system or from solar winds and are made up of protons and charged nuclei in the energy range between 1 MeV and 10 GeV. The SPE consist mainly of protons with kinetic energies below 1 MeV up to a few hundred MeV which are emitted by the sun 5 to 10 times a year. According to Cucinotta et al. (2010) only less than 10% of the SPE would lead to significant health risks for non-protected astronauts, but the occurrence of a SPE cannot be predicted, only detected after the event. The SPE and GCR with energies below 2 GeV are modulated by an eleven-year solar cycle. At solar minimum the solar wind is weakest and the GCR flux is twice as high as at solar maximum. Due to this radiation, an astronaut could be exposed to a total effective dose of more than 1 Sv on a 500-day Mars mission (Shiver, 2008), if radiation protection is neglected. Therefore, risk modeling at doses larger than 1 Gy is important for providing realistic risk estimations for long term exploratory space missions. Currently two main cumulative risk quantities are generally applied for producing radiation related cancer risk estimations. The first quantity, called lifetime attributable risk (LAR), was introduced by Vaeth and Pierce (1990) and is an integration of failure rates (cancer incidence rates in this study) based on the conditional survival probability of a person alive at age at exposure e, to reach at least an attained age a. The survival curves, required in the calculations of LAR, refer to unexposed populations. This feature makes the LAR for cancer

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Table 1
LSS datasets, (obtained from www.rerf.or.jp) used for the analysis with the corresponding follow-up period and given dose information.

Dataset	Cancer	Filename	Follow-up period	Dose information
1	Solid cancer incidence (Grant et al., 2017)	sol_col_2017ext_v1.csv	1958–2009	DS02-R1 neutron RBE = 10 weighted colon dose
2	Solid cancer incidence (Preston et al., 2007)	lssinc07.csv	1958–1998	DS02 different organ doses, separate photon and neutron doses
3	Leukemia incidence (Hsu et al., 2013)	lsshempy.csv	1950–2001	DS02 neutron RBE = 10 weighted bone marrow dose, separate photon and neutron doses

independent of non-cancer excess mortality, where this latter quantity has very large uncertainties. Walsh et al. (2014) noted that the LAR can be used to calculate future cancer risks, but large uncertainties could arise from the assumption that the baseline cancer rates used in the calculation will still be representative for the future population. A second cumulative risk measure introduced by Vaeth and Pierce (1990), is the risk of exposure-induced cancer (REIC). REIC is similar to LAR, except that in the calculation of REIC, survival curves for populations exposed to a dose D are used. Difficulties arise in the specification of a dose dependent survival curve which includes acute mortality after an exposure to several Gy as well as a late radiation induced non-cancer mortality (Kellerer et al., 2001).

In the German software tool ProZES documentation (Ulanowski et al., 2020) it is explained that, in order to obtain the radiation attributed cancer risk for a population of interest (European astronauts in this study), a transfer needs to be applied to the risk obtained from the studied population (The Life Span Study (LSS) of Japanese A-bomb survivors). In general, the excess risk calculation, which is required in the calculation of cumulative risks, can be represented as the weighted sum of the excess absolute risk (EAR) and the excess relative risk (ERR) multiplied with the age and gender specific cancer incidence rates in the population and year of interest. Consequently, a scaling to the LSS EAR can be applied in order to increase the degree of representativeness of EAR to the European astronauts. In this study an EAR baseline scaling, based on the ratio of the baselines between the target and study population, is applied. It is important to note that the differences in the baseline risks are due to national and ethnic factors as well as due to differences in secular trends. In this study, space radiation risk calculations with and without EAR scaling are presented and discussed.

The ICRP (2007) used weights of 0.5 in order to weight the ERR and EAR models for all tissues in the calculation, except for breast and bone marrow, where only an EAR model was applied. Since the exact value of these weights is still under discussion, the cancer incidence risks are calculated in three different ways in this study: just an EAR model, an equally weighted risk model and just an ERR model, to reflect the full range in the uncertainty connected with the choice of EAR and ERR model weightings.

In order to transfer solid cancer risks obtained for A-bomb survivors LSS at high dose-rates to low dose-rates the dose and dose-rate effectiveness factor (DDREF) is included in the solid cancer risk models. The ICRP (2007) recommended a DDREF value of 2, but recent studies, combining direct evidence from many epidemiological studies with a meta-analytic approach (Hoel, 2018; Jacob et al., 2009; Kocher et al., 2018; Shore et al., 2017), have indicated that a value of less than 2 could be more appropriate than 2. Therefore, in this study space radiation risks are calculated with a DDREF of 1.

In the most recent publicly available LSS epidemiological data from the Radiation Effects Research foundation (RERF), website: www.rerf.or.jp, pertaining to solid cancer and leukemia incidence, no information on separate neutron and gamma doses are published. Only the total colon dose including the relative biological effectiveness (RBE) weighted neutron dose is considered. Since the neutron RBE is energy and dose dependent, a fixed RBE of 10 can easily lead to an overestimation of the risk per unit dose. Therefore, in this study an RBE model is developed based on an older LSS dataset from the RERF with less years of follow-up, but where γ- and neutron doses are published separately. This model is then applied to the most recent dataset in order to analyze the impact of the neutron RBE on space radiation protection.

The excess relative (ERR) and absolute (EAR) incidence risks for solid cancer per unit colon dose and leukemia per unit red bone marrow (RBM) dose, which are used to calculate the cumulative risks presented here, are fitted to the atomic bomb survivors LSS data from Hiroshima and Nagasaki for the relevant dose range. Using the same LSS data, the corresponding covariance matrices for the risk model fit parameters are

calculated. An empirical neutron RBE model is applied in order to analyze the influence of a different neutron RBE on risk and the impact of using different risk models and the EAR baseline scaling on the two cumulative risk quantities considered here (LAR and REIC). Finally, cancer incidence risks for a lunar and two Mars missions are estimated with LAR and REIC including a comprehensive Monte-Carlo simulation of uncertainties, using the most recent publicly available epidemiological data from the RERF.

2. Materials and methods

2.1. Atomic-bomb survivors data

Different publicly available LSS epidemiological data from the Radiation Effects Research foundation (RERF), website: www.rerf.or.jp, pertaining to solid cancer (Grant et al., 2017; Preston et al., 2007) and leukemia (Hsu et al., 2013) incidence with either DS02 or DS02R1 doses are analysed. The different datasets are listed in Table 1. For the dataset 1 (Grant et al., 2017) which contains 22,538 first primary solid cancers among 105,444 people with 3.8 person years of follow-up, only the RBE = 10 weighted neutron dose information is given. Dataset 2 (Preston et al., 2007) has 17,448 first primary solid cancers among 105,427 people with 2.8 million person years of follow-up and dataset 3 (Hsu et al., 2013) contains 312 leukemias among 113,011 people with 3.6 million person years of follow-up. In dataset 2 different types of organ doses are available and in datasets 2 and 3 the RBE = 10 weighted colon and RBM doses as well as separate γ- and neutron doses are published. Computations based on dataset 1 for solid cancer risks are performed with respect to the weighted colon doses while computations based on dataset 3 for leukemia risks are based on the weighted RBM doses.

2.2. ERR and EAR risk models

The mathematical forms of the ERR and EAR models applied in this paper are the same as those considered by Schneider and Walsh (2009). The differences between Schneider and Walsh (2009) and the present work are that the most recent LSS incidence data are considered instead of LSS mortality data and that, in order to analyze the impact of the neutron RBE, an empirical model, based on the older dataset 2, is used. To characterize the radiation related solid cancer incidence risk, a linear excess risk (ER - where ER is either ERR or EAR) model is considered and fitted to the data of dataset 1. The risks are factorized into a function of colon dose D_c and a modifying function that depends on the variables attained age a, age at exposure e and gender s.

$$ER_s(D_c, e, a, s) = \beta D_c \mu_s(e, a, s) \tag{1}$$

where β is the initial slope. The subscript S denotes solid cancer and μ_s is the risk effect modifying function:

$$\mu_s(e, a, s) = \exp\left(\gamma_e\left(\frac{e-30}{10}\right) + \gamma_a \log\left(\frac{a}{70}\right)\right)(1 \mp s) \tag{2}$$

where - is used for males and + for females. The fit parameters γ_e, γ_a and s are gender-averaged and centered at an attained age a of 70 years and an age at exposure e of 30 years.

The leukemia incidence excess relative and absolute risks are traditionally fitted to a linear-quadratic dose response model (Hsu et al., 2013), using dataset 3:

$$ERR_L(D_m, e, a, s) = (\beta D_m + \delta D_m^2)\mu_{L1}(e, a) \tag{3}$$

$$EAR_L(D_m, e, a, s) = (\beta D_m + \delta D_m^2)\mu_{L2}(e, a, s) \tag{4}$$

where β and δ are the linear and quadratic dose-response parameters. L denotes leukemia, D_m red bone marrow dose and μ_{L1} and μ_{L2} are the risk effect modifying functions:

$$\mu_{L1}(e, a) = \exp\left(\gamma_e \log\left(\frac{a-e}{40}\right) + \gamma_a \log\left(\frac{a}{70}\right)\right) \tag{5}$$

$$\mu_{L2}(e, a, s) = \exp\left(\gamma_e\left(\frac{e-30}{10}\right) + \gamma_a \log\left(\frac{a}{70}\right)\right)\exp(s) \tag{6}$$

The fit parameters γ_e and γ_a are gender-averaged and centered at an attained age a of 70 years and an age at exposure e of 30 years. The fit parameter s is given for women and set to 0 for men.

2.3. Neutron RBE model

In the most recent dataset 1, with the most years of follow-up, only the total colon doses, including the RBE = 10 weighted neutron dose, are available and no separate information about neutron and gamma doses are published. In order to analyze the influence of different neutron RBEs on cancer risk estimation, a neutron RBE model based on the older dataset 2, where separate neutron and gamma doses were available, is developed. Therefore, the ERR and EAR models for solid cancer and leukemia shown in the Appendix A are fitted with respect to organ averaged dose to the A-bomb survivor data for six different neutron RBEs: 10, 35, 60, 80, 100 and the dose dependent RBE from Sasaki et al. (2006). The resulting fit parameters are shown in the Appendix B in Tables B1–B4.

In order to fit the risks as function of RBE, the mean neutron dose weighted RBE, calculated from the dose dependent RBE from Sasaki et al. (2006), needs to be determined using the neutron RBM from the grouped LSS data in each cell containing person years at risk:

$$RBE_{Sasaki} = \frac{\sum_{Person\ years} D_n^{person\ years} RBE(\gamma, D_n{}^{person\ years})}{D_n^{tot}} \tag{7}$$

where $D_n^{person\ years}$ denotes the neutron dose for each cell in the grouped LSS data, D_n^{tot} the total neutron dose of all cells in the grouped publicly available A-bomb LSS data and the neutron dose dependent RBE is taken from Sasaki et al. (2006):

$$RBE(\gamma, D_n) = \frac{2(\vartheta_n + D_n)}{\vartheta_\gamma + \sqrt{\vartheta_\gamma{}^2 + 4(\vartheta_n + D_n)D_n}} \tag{8}$$

with the crossover dose ϑ:

$$\vartheta = \frac{\alpha}{\beta} \tag{9}$$

The kerma-weighted α-coefficient for γ-rays at 5 cm depth is $1.549 \times 10^{-2}\mathrm{Gy}^{-1}$ and for neutrons it is $119.334 \times 10^{-2}\mathrm{Gy}^{-1}$. The β-coefficient is 5.355×10^{-2}/Gy for both neutrons and γ-rays. With this method the mean neutron dose weighted RBE from Sasaki is found to be 25 from dataset 2.

The neutron RBE model is fitted separately for solid cancers f_S and leukemia $f_{L1/L2}$:

$$ER_s(D_c, e, a, s, RBE) = ER_s(D_c, e, a, s) f_S(RBE) \tag{10}$$

$$ER_L(D_m, e, a, s, RBE) = (\beta f_{L1}(RBE) D_m + \delta f_{L2}(RBE) D_m^2)\mu_{L1/L2}(e, a) \tag{11}$$

Where $ER_s(D_c, e, a, s)$ is the excess risks from Eq. (1) and $\mu_{L1/L2}(e, a)$ are the risk effect modifying functions of Eqs. (5) and (6). Since the fit parameters for the attained age, age at exposure and gender risk effect modifiers obtained with dataset 2 for solid cancer and dataset 3 for leukemia, shown in the Appendix B in Tables B1–B4, only vary slightly with RBE, they are assumed to be constant and the values for RBE = 10 are used for the modeling. The ratios of the main risk to dose response fit parameters (e.g., the β in Eq. (1)) at different RBEs to the risk to dose response fit parameter of RBE = 10 for solid cancer and leukemia at 1 Gy, shown in the Appendix B in Tables B1–B4, are then plotted as a function of RBE and the uncertainties are calculated with a Gaussian error propagation using the individual fit parameter variances shown in

Table 2
Results of fitting a linear and an exponential model for solid cancer and a quadratic exponential model for leukemia to the ratio of the risk to dose response fit parameters in Tables B1–B4 shown in the Appendix B and the risk to dose response fit parameter for neutron RBE = 10. For leukemia only the results for the quadratic dose term are shown, since for the linear dose term no neutron RBE dependence was found.

Linear model		
Risk	Solid cancer	Leukemia
ERR	−0.0060 ± 0.0003	−0.0136 ± 0.0017
EAR	−0.0059 ± 0.0003	−0.0133 ± 0.0016
Exponential model		
Risk	Solid cancer	Leukemia
ERR	−0.0079 ± 0.0002	−0.0014 ± 0.0003
EAR	−0.0077 ± 0.0002	−0.0012 ± 0.0002

Table 2. Then two different models are considered to fit the data points. For solid cancer and leukemia, a linear model is considered for the excess risk:

$$f_{S/L}(RBE) = \alpha(RBE - 10) + 1 \tag{12}$$

as well as an exponential approach for solid cancer:

$$f_S(RBE) = \exp(\alpha(RBE - 10)) \tag{13}$$

And for leukemia:

$$f_L(RBE) = \exp(\alpha(RBE - 10)^2) \tag{14}$$

where α denotes the fit parameter, the subscripts S and L denote solid cancer and leukemia respectively.

2.4. LAR

The method of Kellerer et al. (2001) is applied here to obtain LAR:

$$LAR(e) = \int_{e+l}^{a} h_S(a, e, D)\frac{S(a)}{S(e)}da + \int_{e+l}^{a} h_L(a, e, D)\frac{S(a)}{S(e)}da \tag{15}$$

where a denotes the attained age, e the exposed age and l the minimum latency period (5 years for solid cancer, 2 years for leukemia). The excess cancer incidence risk for solid cancer can be written as:

$$h_S(a, e, D) = \frac{w_{S1}ERR_S(D, a, e)m_S(a) + w_{S2}EAR_S(D, a, e)/10,000}{DDREF} \tag{16}$$

while for leukemia the excess cancer incidence risk is given by:

$$h_L(a, e, D) = w_{L1}ERR_L(D, a, e)m_L(a) + \frac{w_{L2}EAR_L(D, a, e)}{10,000} \tag{17}$$

where $m_S(a)$ and $m_L(a)$ are the baseline cancer incidence rates from Germany for solid cancer and leukemia respectively, used to be representative for European astronauts. The rates are calculated by taking the mean of the incidence rates from the website www.krebsliga.de from 2010 to 2016. The ERR and EAR are the excess relative and absolute risks from Eqs. (1), (3) and (4). The fit parameters of the EAR were calculated per 10,000 PY Gy, which is accounted for by the factor 10,000 in the Eqs.(16) and (17). For solid cancer, the excess risks are weighted with the weights w_{S1} and w_{S2} and for leukemia with the weights w_{L1} and w_{L2}. $S(a)$ is the survival curve from Kellerer et al. (2001) for the unexposed population:

$$S(a) = \exp(c_1(1 - \exp(c_2 a))) \tag{18}$$

with $c_1 = 0.0015$, $c_2 = 0.0820$ for males and $c_1 = 0.0005$, $c_2 = 0.0905$ for females. The ratio of the two survival curves in Eq. (15) describes the conditional probability of a person to reach at least age a when having been alive at age e. In this study all cumulative risks are calculated up to an attained age a of 89 years.

2.5. REIC

To obtain REIC the method to calculate the risk of exposure induced death (REID) from Schneider and Walsh (2009), which is based on the methods introduced by Kellerer et al. (2001), is applied with the adaptation to calculate cancer incidence instead of mortality:

$$REIC(e, D) = \int_{e+l}^{a} h_S(a, e, D)\frac{S(a, D)}{S(e, D)}da + \int_{e+l}^{a} h_L(a, e, D)\frac{S(a, D)}{S(e, D)}da \tag{19}$$

where h_S and h_L are the excess cancer incidence risks for solid cancer Eq. (16) and leukemia Eq. (17) respectively. The attained age in years is denoted by a, e is the age at exposure in years, l the minimum latency period. The ratio of the survival curves of the population after an exposure to a dose D is described by:

$$\frac{S(a, D)}{S(e, D)} = \frac{S(a)}{S(e)}(1 - NCM(D))(1 - ARM(D)) \tag{20}$$

where $S(a)$ is the survival curve of the unexposed population from Eq. (18). The $NCM(D)$ is the excess relative non-cancer mortality. It accounts for late radiation induced non-cancer mortality, such as cardiac mortality for doses higher than 0.5 Gy. For each Gy a factor of 0.1 is added to the quantity. From Anno et al. (2003) the acute radiation-induced mortality (ARM) is taken as:

$$ARM(D) = \frac{1}{2}\left(\mathrm{erf}\left(\frac{k + 7.133\log(D)}{\sqrt{2}}\right) + 1\right) \tag{21}$$

where k accounts for the application of medical care. If no medical care is applied $k = -4.4011$ and if medical care is applied $k = -5.6571$. In this study only results for no medical care are presented and discussed.

2.6. Dose scale

Computations of solid cancer risk are based on the weighted colon dose, while the computations of leukemia risks are performed with respect to the weighted RBM dose. Since the energies of space radiation are very high, one can assume that the colon and the RBM doses will be equal for a given fluence at first order. Therefore, in this study, the total cancer risk is calculated by simply adding up the calculated solid cancer and leukemia risks.

2.7. EAR baseline scaling

In order to obtain the radiation attributed cancer risk for European astronauts a transfer needs to be applied to the risk obtained for the studied population of Japanese A-bomb survivors (Ulanowski et al., 2020) since the Japanese baseline at calendar $year = 1945 - e + a$ may not be representative of the baseline for European astronauts in 2020, due to, among other factors, secular trends and racial differences in cancer rates. Here this transfer is realized by an EAR baseline scaling as described by Ulanowski et al. (2020) where the ratio of the baseline incidence rates of Germany $m(a)_G$ and Japan $m(a)_J$ is used as a scaling factor:

$$EAR_G(D, e, a, s) = EAR_J(D, e, a, s)\frac{m(a)_G}{m(a)_J} \tag{22}$$

The internal baseline from the LSS cohort of A-bomb survivors in Japan has a major contribution from the first dose group of 1–5 mGy in the epidemiological data. This baseline yields uncertainties, because a few of the cancers in this group could be radiation related excess, but it is not known which ones. Therefore, the ratio of the excess absolute risk and the excess relative risk is used to define the internal baseline from the LSS cohort of A-bomb survivors in Japan in this study:

$$\frac{EAR(D, e, a, s)}{ERR(D, e, a, s)} = m(a)_J \quad (23)$$

2.8. Uncertainties

In order to estimate the uncertainties on the LAR and REIC central estimates, Monte Carlo simulations are used to provide appropriate confidence intervals on the central estimates. The uncertainties of the fit parameters (for the dose-response and the risk effect modifiers) are included by Monte-Carlo sampling involving 1000 realisations of these parameters according to the corresponding elements of the parameter covariance matrix. The uncertainties of the German baseline incidence rates are assumed to be Poisson distributed, and also sampled accordingly, with 1000 realisations. From the combined simulations the 95% confidence interval is considered to represent the uncertainty. Since no uncertainties were given with the published fit-parameters for the NCM and ARM models, these uncertainties could not be accounted for in the Monte-Carlo treatment of uncertainties.

3. Results

3.1. Neutron RBE model

In Fig. 1 the ratios of the dose fit parameter at RBE 10, 25, 35, 60, 80 and 100 and the dose fit parameter at neutron RBE 10 are shown with the different fits from Eqs. (12) to (14). The model fit parameters are listed in Table 2. Due to the large uncertainty in the model parameters the ratio of the linear dose parameter for solid cancer and the ratio of the quadratic dose parameter for leukemia, can be fitted with the linear model as well as with the exponential model. Since the exponential model fits the data slightly better and it will not take negative values for even higher RBE values, the further analysis is executed with this model. The linear dose-response parameter β for leukemia does not show any RBE dependence for both excess risks. Consequently, no model is applied.

3.2. ERR and EAR risk models

Fitting the ERR and EAR models Eqs. (1)–(4) to the Japanese atomic bomb survivor data yields the model fit parameters in Tables B6 and B7 and the corresponding covariance matrices in Tables B8–B11 shown in Appendix B. In Fig. 2 LAR and REIC are calculated with an equally weighted excess risk model as a function of dose with and without EAR scaling for men, using a neutron RBE of 10 and an exposed age of 41 years. The 95% confidence interval is also calculated and shown by dashed lines. In Fig. C1 in the Appendix C the results for the same set up are shown for women. LAR and REIC increase both with dose and women have in general a higher cancer incidence risk than men. Using the equally weighted excess risk model and no EAR baseline scaling women exposed to 1 Gy at age 41 years have a 4.7% higher LAR and a 4.3% higher REIC than men. Including EAR scaling the LAR for women rises by 3.7% and the REIC by 3.3% compared to no scaling and for men the LAR with the scaled EAR is 2.8% higher than without, while REIC increases by 2.6%. In Fig. 2 the neutron RBE-dependence of LAR and REIC for the different scenarios of EAR scaling for men and in Fig. C1 the results for women are shown. The results are calculated for an exposure of 1 Gy at an age of 41 years using the developed neutron RBE model and the equally weighted excess risk model. Both risks decrease with increasing neutron RBE. Using a RBE of 100 instead of 10 decreases the risks by almost 50%. Additionally, the results for LAR and REIC for every scenario of EAR scaling for an exposure of 1 Gy colon dose and a neutron RBE of 10 as function of exposed age for men is shown in Fig. 2 and for women in Fig. C1. Both risks decrease with increasing age at exposure. In Fig. 3 REIC and LAR are calculated with an EAR model as function of dose, neutron RBE and exposed age for men and in Fig. 4 the risk estimations are shown, calculated with an ERR model. The equivalent figures for women Figs. C2 and C3 can be found in the Appendix C. Using the ERR model the EAR scaling cannot be applied. The results calculated including EAR scaling with the EAR model and the equally weighted excess risk model and the ERR results are almost equivalent and show only small differences in the uncertainties. For men, LAR without EAR scaling is 2.8% smaller calculated with the EAR model than calculated with the equally weighted model and 3.7% smaller for women. For REIC the risks decrease by 2.5% and 3.3% for men and women respectively.

4. Discussion

4.1. Neutron RBE

Different studies found indications that the neutron RBE for A-bomb survivors is higher than the traditionally used RBE of 10. Kellerer et al. (2006) analysed the LSS data and estimated the neutron RBE to be 100. Rühm and Walsh (2007) calculated the RBE according to the ICRP 60 recommendations and found it to be 40.2 at 500 m and 25.1 at 2000 m distance to the epicenter. Satoh et al. (2018) evaluated the log-likelihood at several RBE values in the range of 5–120 for A-bomb survivors from Hiroshima and from the LSS (Hiroshima and Nagasaki) separately and found the values 65 and 75 respectively. Walsh (2013) applied a hierarchical partitioning approach to calculate a neutron RBE directly from the LSS all solid cancer ERR fit parameters per unit colon dose and reported an RBE of 65 (95% CI: 11; 170). Applying a similar approach to Walsh (2013) but with more recent data, Cordova and Cullings (2019) calculated different RBEs for different organs based on the LSS data. The RBE for colon dose was found to be 80 and for other types of organ doses, between 25 and 60. Additionally, Cordova and Cullings (2019) agreed with previous statements in Kellerer et al. (2006) by stating that since the colon is among the deepest of organs it may not be the best organ dose type to use for the RBE estimations, since colon doses minimize the role of neutrons due to the high body shielding of the colon. Using a higher neutron RBE than the fixed RBE of 10 has a huge impact on the risk estimates. For an exposure of 1 Gy at an age of 41 years using a neutron RBE of 10, equally weighted excess risks and no EAR baseline scaling, LAR for a woman is 16.2% (13.7; 19.0) and REIC is 14.6% (12.3; 17.1). For men the risks are 11.5% (9.4; 14.0) and 10.3% (8.4; 12.6) respectively. If a neutron RBE of 80 is used the risks decrease for women to 9.2% (7.6; 10.9) and 8.3% (6.8; 9.8) for LAR and REIC respectively and for men to 6.4% (4.9; 8.0) and 5.7% (4.4; 7.2). Consequently, the risks decrease by almost 50% for a higher neutron RBE. However, it has to be noted that the RBE dependence in this study is calculated with an empirical neutron RBE model, ideally the separate neutron and gamma doses for a selection of organs are required with all the publically available LSS data.

4.2. EAR baseline scaling

The EAR baseline scaling described by Ulanowski et al. (2020) is included in this study in order to transfer the risks obtained for the studied population (Japanese A-bomb survivors) to European astronauts. Using the scaled EAR has a strong impact on the space radiation risk calculation. For the missions considered in this study, the doses are in the cSv range and the maximum increase of the cancer risk due to scaling is 8.1%. In Figs. 2 and 3 a dose dependence can be observed. For LAR the difference increases with dose while for REIC the largest difference can be found in the dose range from 1 to 3.5 Gy. With regard to possible long-term exploratory space missions in the future, where astronauts are exposed to higher doses, the impact of the EAR baseline scaling needs to be considered.

Nevertheless, it has to be noted that the use of such a scaling is still being discussed, because on the one hand it is not clear whether the

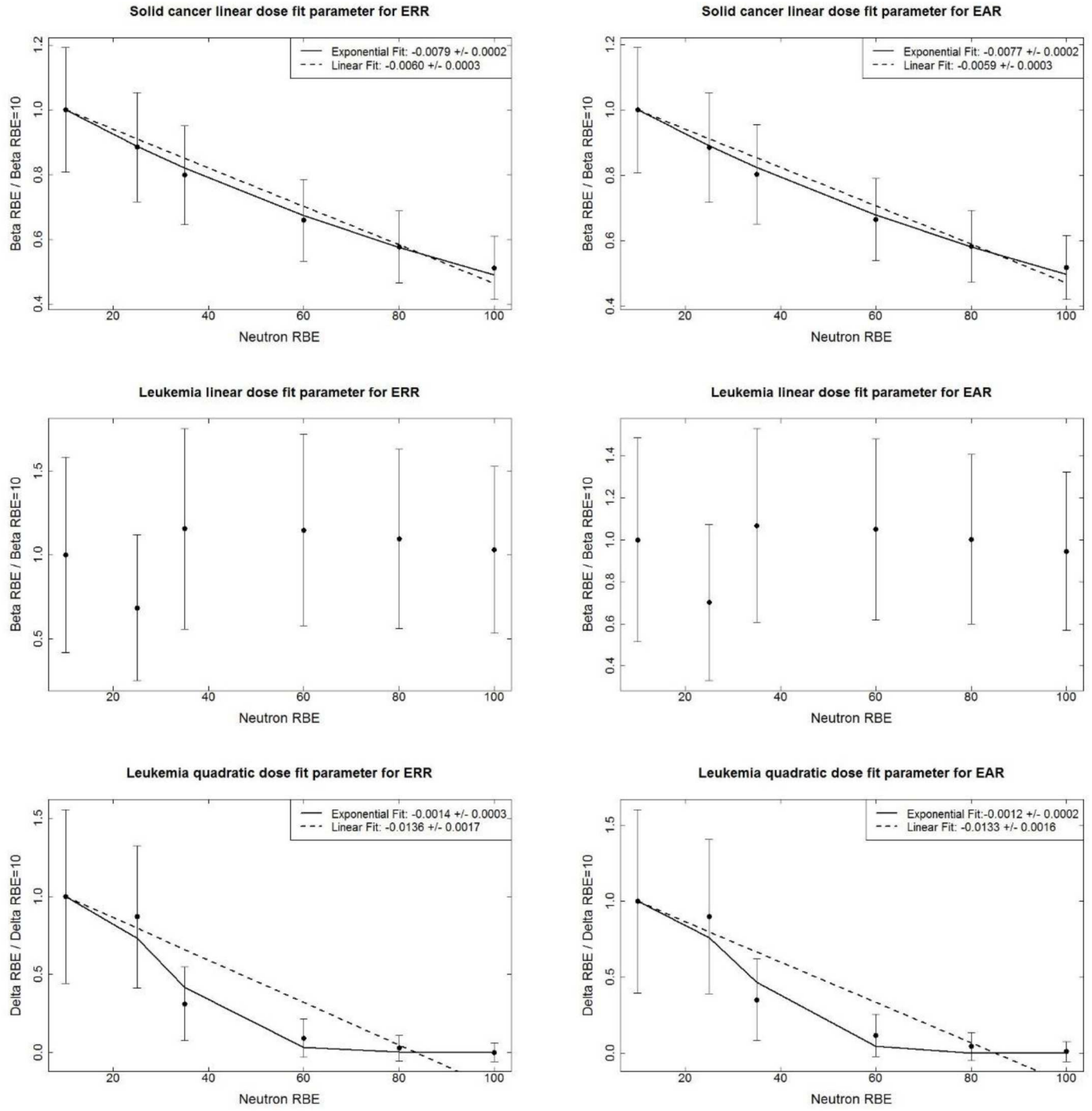

Fig. 1. The black points show the ratio of the different dose fit parameters from dataset 2 for solid cancer and dataset 3 for leukemia at different RBEs (10, 25 (Sasaki), 35, 60, 80, 100) and the dose fit parameter at RBE = 10 as function of the neutron RBE. The uncertainties are calculated with a Gaussian error propagation using the variances shown in the Appendix B in Table B5. The solid line shows the exponential fit and the dashed line the linear fit. All other fit parameters are assumed to be constant.

transfer of the absolute radiation induced cancer risk between two populations can be described by considering the differences in the baseline of these populations, since the origin of these risks are different. Baseline cancer incidence rate differences are due to environmental influences and lifestyle choices, while for the excess absolute risk the origin of the mutations is radiation. On the other hand, the differences in the baselines are already taken into account in the calculation by considering a weighting between relative and absolute excess risks.

4.3. Excess risk models

The ICRP (2007) recommended to use a 50:50 weighting for the excess risks to calculate the cumulative incidence risks for almost every cancer site. Only for breast cancer and bone marrow is a pure EAR model recommended. Nevertheless, there are still discussions going on (Walsh and Schneider, 2012; Little and Wakeford, 2012; Pawel and Gilbert, 2012), about which weights should be used. In this study the risks calculated with the 50:50 weighting of the excess risks are compared to the risks calculated with the two extreme cases of applying a

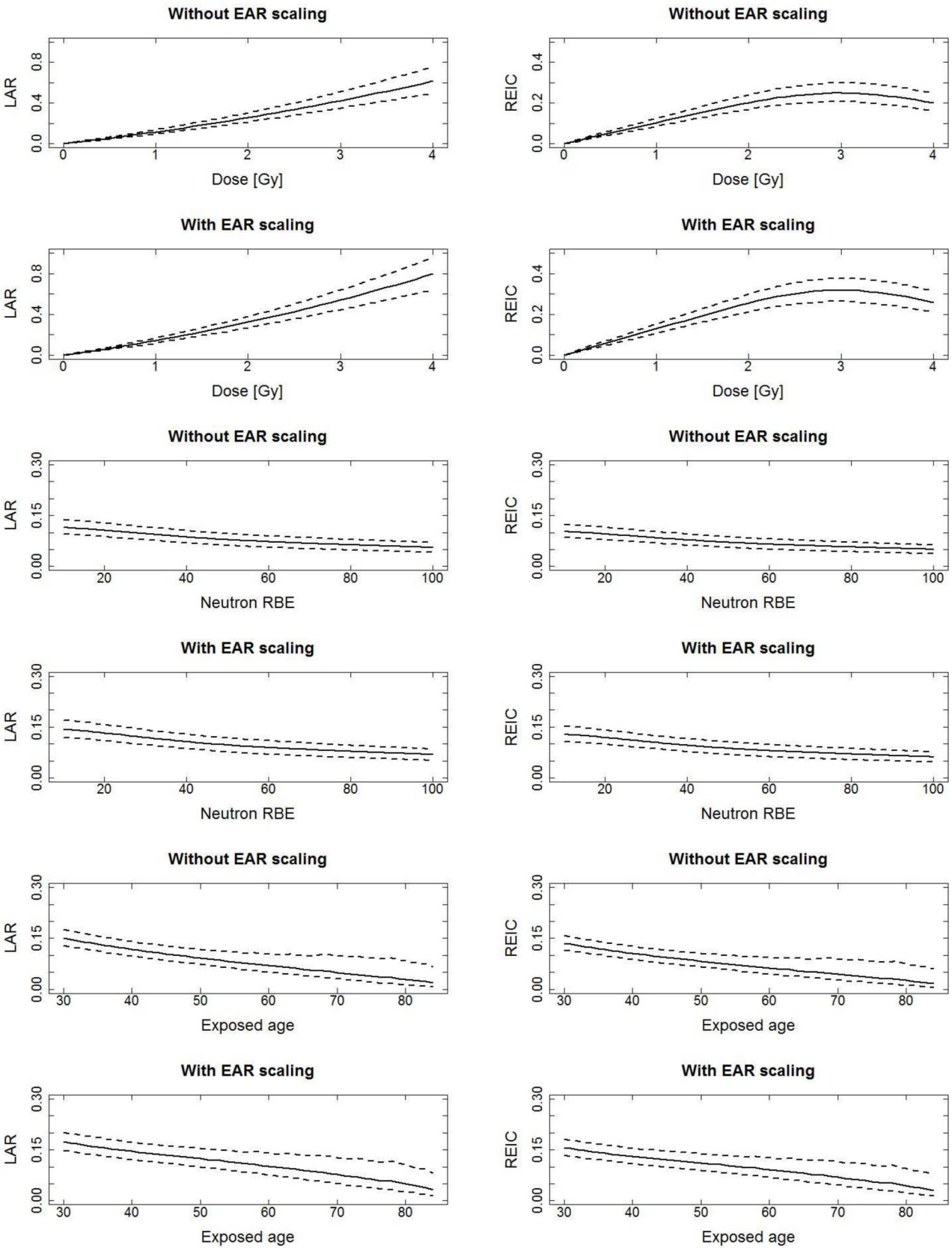

Fig. 2. Results for LAR and REIC in decimals calculated for *men* as function of dose, neutron RBE and exposed age for a dose of 1 Gy, a neutron RBE of 10 at an exposed age of 41 years are shown with and without EAR baseline scaling. The risks are calculated with *equally weighted excess risks*. The solid line corresponds to the central estimate and the dashed lines show the 95% confidence interval. Note: the very large uncertainties in the radiation dependant acute mortality in the survival curves above 2 Gy, are not included in the results for REIC).

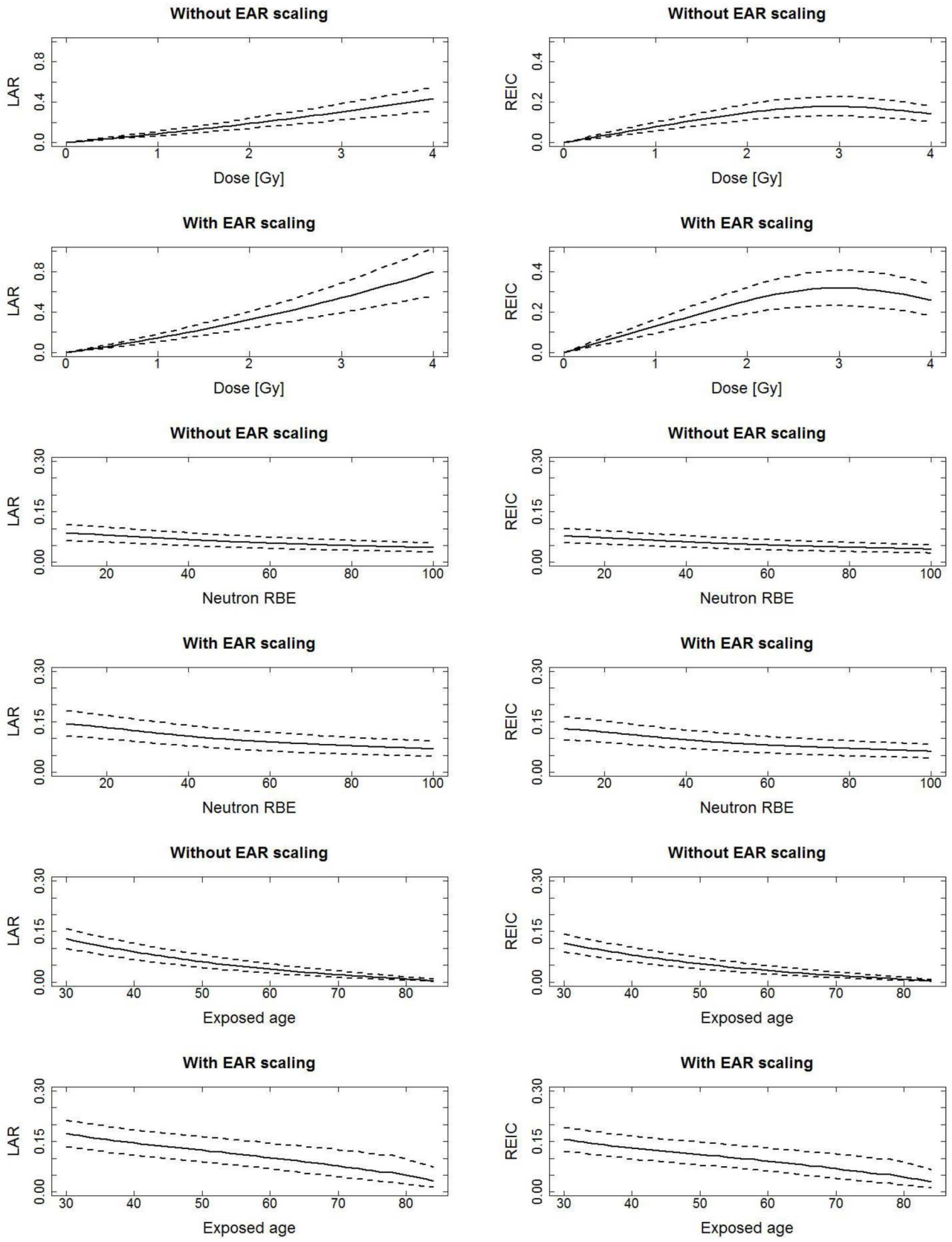

Fig. 3. Results for LAR and REIC in decimals calculated for *men* as function of dose, neutron RBE and exposed age for a dose of 1 Gy, a neutron RBE of 10 at an exposed age of 41 years are shown with and without EAR baseline scaling. The risks are calculated with *an EAR model*. The solid line corresponds to the central estimate and the dashed lines show the 95% confidence interval. Note: the very large uncertainties in the radiation dependant acute mortality in the survival curves above 2 Gy, are not included in the results for REIC).

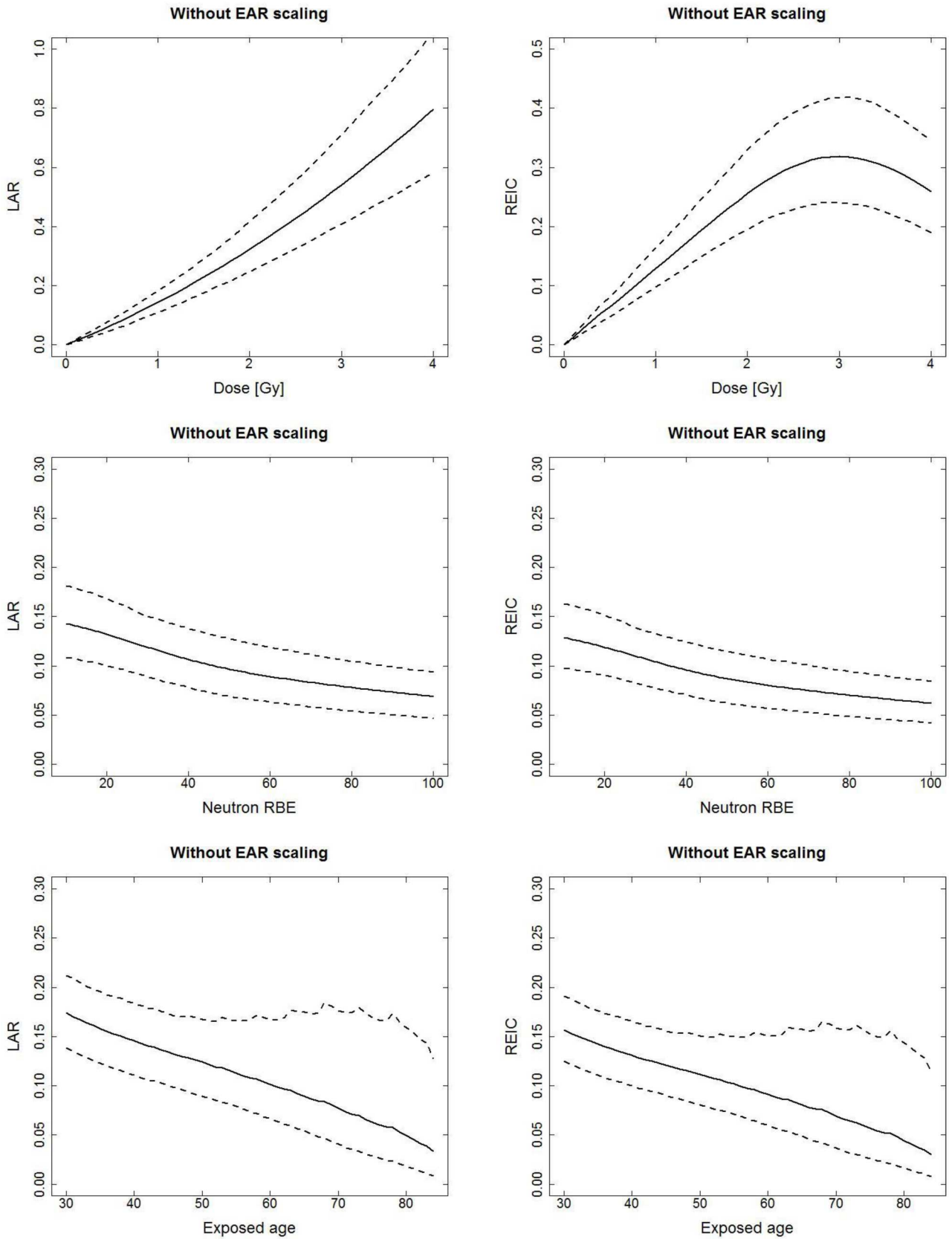

Fig. 4. Results for LAR and REIC in decimals calculated for *men* as function of dose, neutron RBE and exposed age for a dose of 1 Gy, a neutron RBE of 10 at an exposed age of 41 years are shown without EAR baseline scaling. The risks are calculated with *an ERR model*. The solid line corresponds to the central estimate and the dashed lines show the 95% confidence interval. Note: the very large uncertainties in the radiation dependant acute mortality in the survival curves above 2 Gy, are not included in the results for REIC).

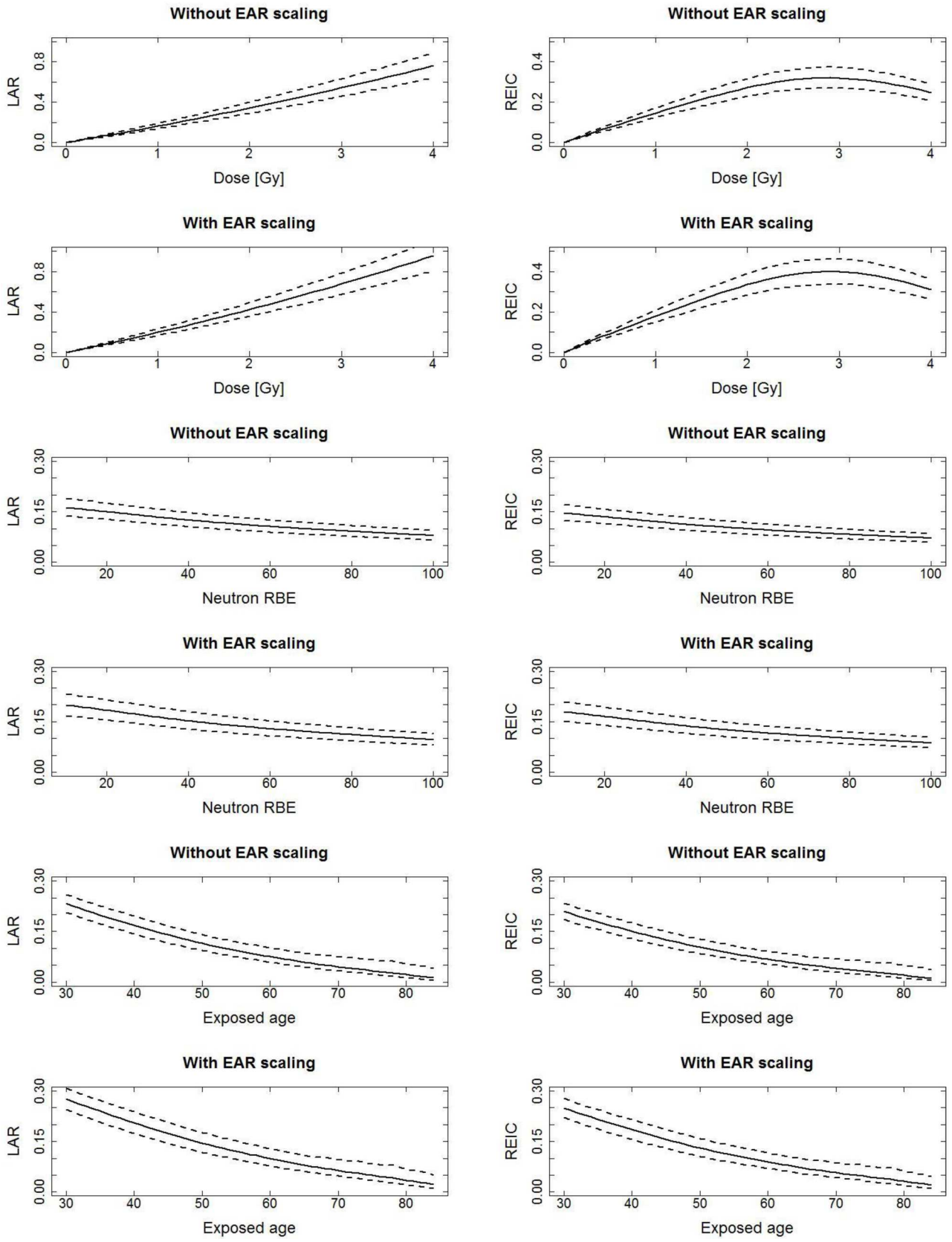

Fig. C1. Results for LAR and REIC in decimals calculated for *women* as function of dose, neutron RBE and exposed age for a dose of 1 Gy, a neutron RBE of 10 at an exposed age of 41 years are shown with and without EAR baseline scaling. The risks are calculated with *equally weighted excess risks*. The solid line corresponds to the central estimate and the dashed lines show the 95% confidence interval. Note: the very large uncertainties in the radiation dependant acute mortality in the survival curves above 2 Gy, are not included in the results for REIC).

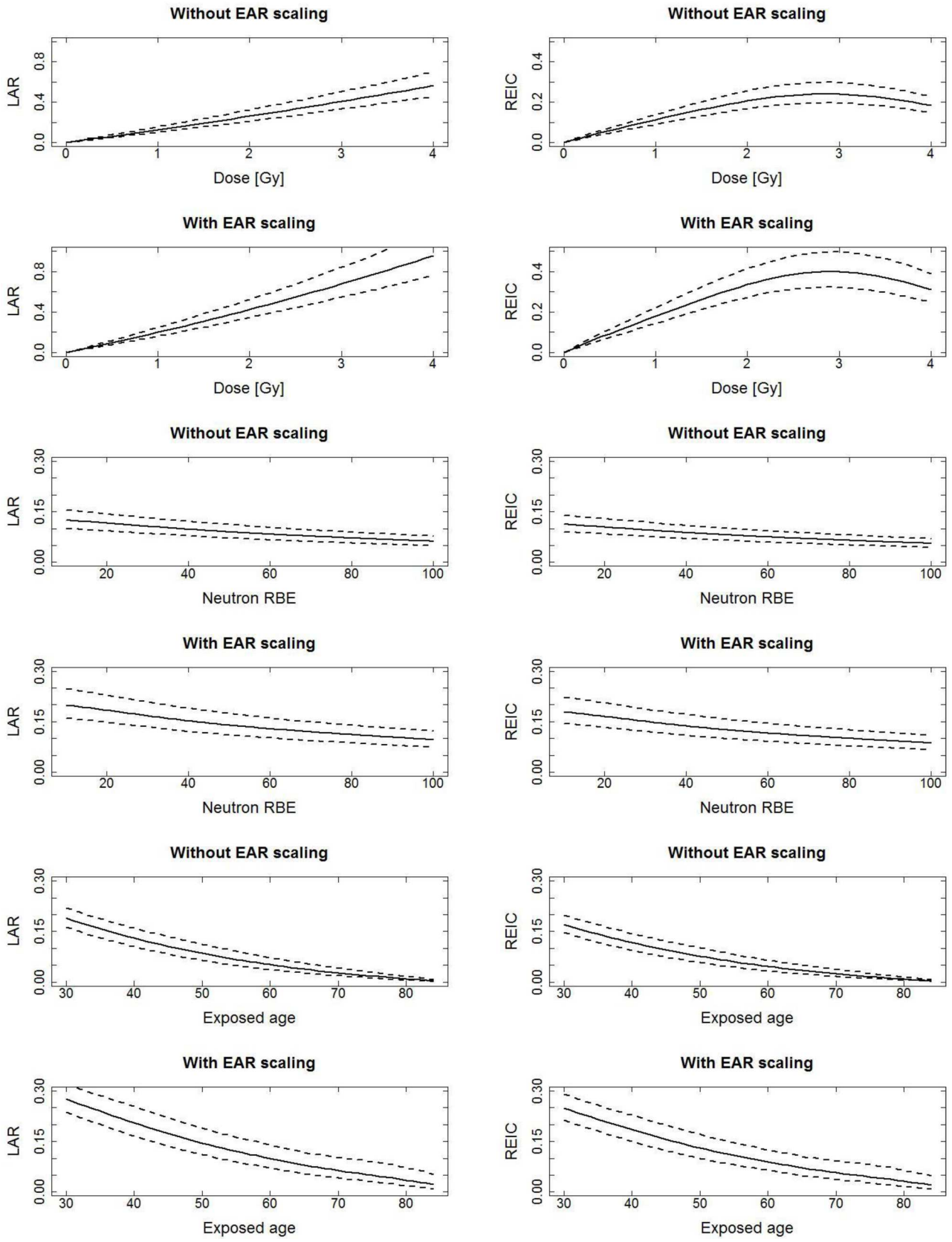

Fig. C2. Results for LAR and REIC in decimals calculated for *women* as function of dose, neutron RBE and exposed age for a dose of 1 Gy, a neutron RBE of 10 at an exposed age of 41 years are shown with and without EAR baseline scaling. The risks are calculated with *an EAR model*. The solid line corresponds to the central estimate and the dashed lines show the 95% confidence interval. Note: the very large uncertainties in the radiation dependant acute mortality in the survival curves above 2 Gy, are not included in the results for REIC).

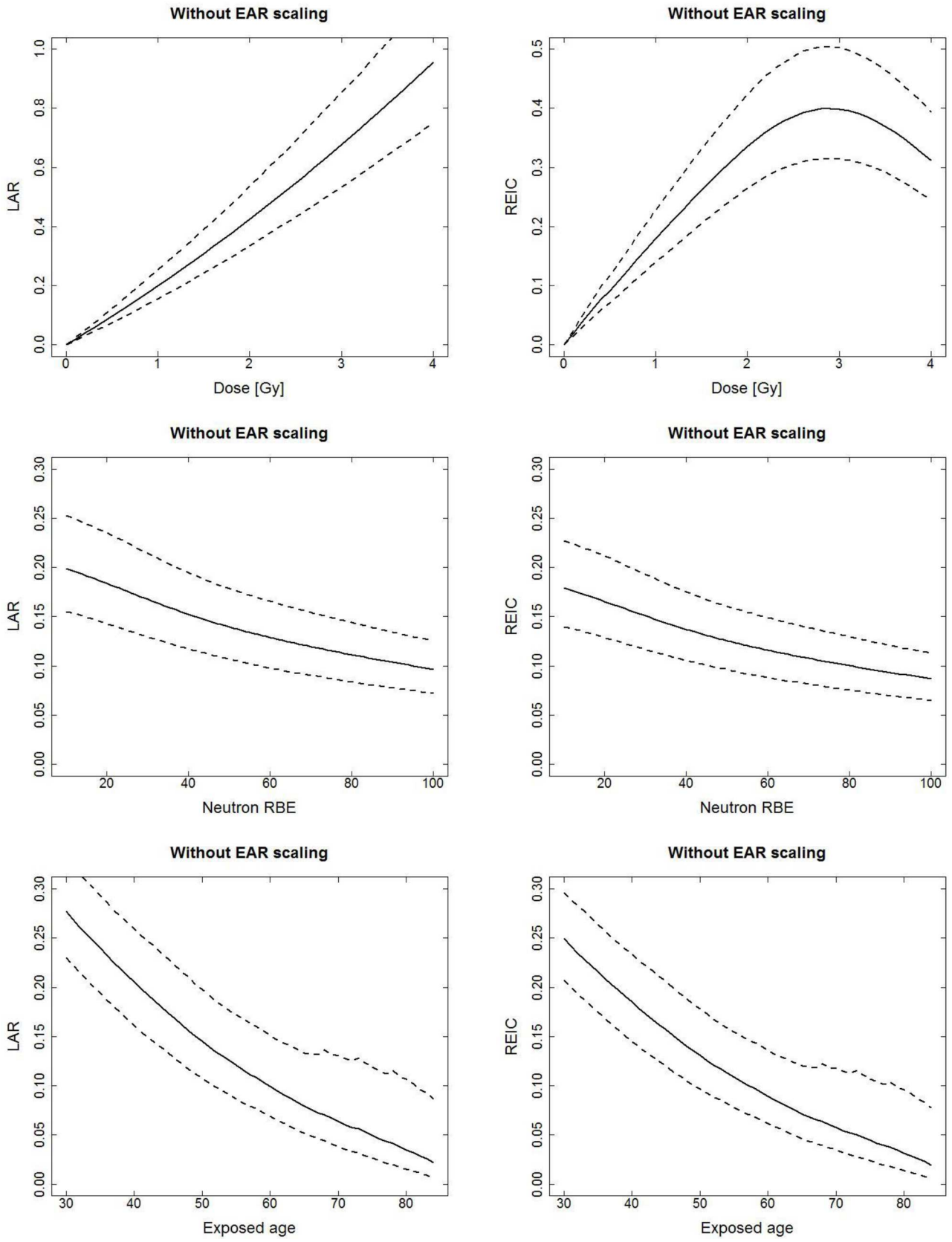

Fig. C3. Results for LAR and REIC in decimals calculated for *women* as function of dose, neutron RBE and exposed age for a dose of 1 Gy, a neutron RBE of 10 at an exposed age of 41 years are shown without EAR baseline scaling. The risks are calculated with *an ERR model*. The solid line corresponds to the central estimate and the dashed lines show the 95% confidence interval. Note: the very large uncertainties in the radiation dependant acute mortality in the survival curves above 2 Gy, are not included in the results for REIC).

pure EAR- and a pure ERR model. In the missions considered, using an EAR model instead of an equally weighted excess risk model leads to a decrease of the risk of between 0.4% and 4.1% if no EAR baseline scaling is applied. If EAR baseline scaling is included, the calculated risks with the EAR- and the equally weighted model, as well as the risks calculated with the ERR model are almost identical and only small differences in their uncertainties are visible.

4.4. DDREF

In this study the risks are calculated with a DDREF of 1, nevertheless one has to keep in mind that including a DDREF of 2 as recommended by the ICRP (2007) for solid cancers in the calculations would reduce the risk estimates for lunar and Mars missions by almost 50%. This large impact is mostly due to the fact that in this dose range the leukemia risk does not contribute much to the total risk estimation, because it rises almost quadratic with dose. For larger doses the impact of the DDREF will therefore be smaller. Direct evidence from epidemiology may be considered to guide the choice of which DDREF value is currently the most appropriate to apply. Several recent, all solid cancer meta-analysis studies (Hoel, 2018; Jacob et al., 2009; Kocher et al., 2018; Shore et al., 2017), have aimed to provide such direct evidence on the magnitudes of a dose-rate effectiveness factor (DREF) by analyzing published risk results from many epidemiological studies with different dose-rates. Table 4 provides a summary of the DREF results from these studies. The first meta-analysis in Table 4 by Jacob et al. (2009) was recently updated (Shore et al., 2017) to include 22 low-dose and/or low dose rate solid cancer studies (19 mortality studies and 3 incidence studies). Another analysis of the DREF was based on a much less comprehensive selection of studies (Kocher et al., 2018) when compared with the wider range of studies considered recently by Shore et al. (2017) and by Hoel (2018) in their assessments of the DREF. Table 4 shows that the evidence for DREF of 1 or 2, depends strongly on the types and numbers of epidemiological studies considered, with the lower values being obtained when one influential study (the Mayak study) was not included in the meta-analysis estimators of DREF. The dependency on the included studies in the analysis has also been observed by Haley et al. (2015) by re-estimating the DDREF including 15 animal studies considering acute and protracted exposures. Including the animal data, they found the DDREF to be in the range of 4.8 to infinity. Also, Tran and Little (2017) aimed to provide an estimate on the low-dose extrapolation factor (LDEF) and DREF by analysing animal data. They found the central estimate of the DREF for gamma exposure with malignant outcomes to be in the range of 1.2–2.3 and the LDEF to be 1.2 for all solid cancers for most malignant outcomes. A LDEF of more than 1 was also implied by Little et al. (2020) by estimating the dose-response curvature for malignant outcomes, which would be consistent with the recommended ICRP DDREF of 2. From these results it can be seen that the current direct evidence from animal and epidemiological studies is not strong enough to confidently guide the choice of whether to apply a DDREF of 1 or 2. Therefore, based on the current state of knowledge, it is important to keep different DDREF values under consideration in the astronaut cancer risk assessments.

4.5. Cancer risk calculation methods for space missions

In order to calculate the radiation related cancer risk, two different cumulative risk measures are used in this study. In the calculation of REIC, late radiation induced non-cancer mortality is accounted for in the survival curves. These deterministic non-cancer risks are modelled based on data of the general population, but since astronauts are very sportive, healthy and non smokers, they are not representative for this group. It can therefore be that due to their excellent physical condition, astronauts are less sensitive to radiation induced non-cancer health risks (e.g. cardiac attacks) and the deterministic risk model would be different for this atypical occupational group. Using nevertheless the models based on the general population may therefore lead to an underestimation of the cancer incidence risk for astronauts at high doses. Since LAR does not account for late radiation induced non-cancer mortality it may be the more appropriate risk assessment method to calculate cancer incidence risks for astronauts, since it avoids a possible underestimation of the risk. Nevertheless, it is important to point out that both risk calculations are based on survival curves, either of the unexposed or exposed population, which are amongst the most uncertain quantities in the calculation. Another method, particularly useful for risk assessments in highly atypical exposed groups such as astronauts (see Walsh et al., 2019a), that reduces the dependence of radiation related risk assessments on population statistics and survival curves (Ulanowski et al., 2019), has recently been published. Current work is underway to include a consideration of this new method (Ulanowski et al., 2019) into the types of analyses presented here.

The NASA (Cucinotta et al., 2007) specified that the risk of exposure induced death (REID) shall not exceed 3% at the 95% upper confidence level. Considering the lethality factors for different cancers in Table A.4.5 of the ICRP 103 report (2007) and weighting them with the cancer case counts of the A-bomb survivor data, a lethality factor of 0.49 can be found for all cancers. Taking this lethality factor into account, the limit for REIC and LAR can be set to be 6.1%. In Table 3 the radiation related cancer risks are calculated for both genders for a 180 days lunar mission, a Mars swing-by and a Mars surface mission at solar minimum for different scenarios of risk models and EAR baseline scaling including the uncertainties. The upper 95% of the confidence

Table 3
Results for LAR and REIC for all cancer in% for different mission types and doses using models based on dataset 1 including the 95% CI. All results are calculated for an age at exposure of 40 years, a neutron RBE of 10 and a DDREF of 1.

		ERR based model W/o EAR scaling		Equally weighted ERR/EAR model W/o EAR scaling		With EAR scaling		EAR based model W/o EAR scaling		With EAR scaling	
Mission	E/Sv	LAR	REIC	LAR	REIC	LAR	REIC	LAR	REIC	LAR	REIC
Males											
Lunar, 180 d	0.17	2.2 (1.6;2.9)	2.2 (1.6;2.9)	1.8 (1.5;2.2)	1.8 (1.5;2.2)	2.2 (1.8;2.7)	2.2 (1.8;2.7)	1.4 (1.0;1.9)	1.4 (1.0;1.9)	2.2 (1.6;2.9)	2.2 (1.6;2.9)
Mars, swing-by 600 d	1.03	15.0 (11.4;19.4)	13.5 (10.2;17.4)	12.2 (10.0;14.7)	10.9 (9.0;13.2)	15.0 (12.5;18.0)	13.5 (11.2;16.2)	9.3 (6.9;12.0)	8.3 (6.2;10.8)	15.0 (11.4;19.2)	13.5 (10.2;17.2)
Mars, exploration 1000 d	1.07	15.7 (11.9;20.2)	14.0 (10.7;18.1)	12.7 (10.4;15.3)	11.3 (9.3;13.7)	15.7 (13.0;18.8)	14.0 (11.6;16.8)	9.7 (7.2;12.5)	8.6 (6.5;11.2)	15.7 (11.9;20.0)	14.0 (10.6;17.9)
Females											
Lunar, 180 d	0.17	3.3 (2.6;4.2)	3.3 (2.6;4.2)	2.7 (2.3;3.2)	2.7 (2.3;3.2)	3.3 (2.8;3.9)	3.3 (2.8;3.9)	2.1 (1.7;2.7)	2.1 (1.7;2.7)	3.3 (2.6;4.1)	3.3 (2.6;4.1)
Mars, swing-by 600 d	1.03	21.2 (16.9;26.3)	19.1 (15.2;23.6)	17.3 (14.8;20.4)	15.6 (13.3;18.3)	21.2 (18.2;24.8)	19.1 (16.3;22.2)	13.4 (10.7;16.5)	12.1 (9.6;14.8)	21.2 (17.0;26.1)	19.1 (15.3;23.4)
Mars, exploration 1000 d	1.07	22.1 (17.6;27.4)	19.8 (15.7;24.5)	18.1 (15.4;21.2)	16.1 (13.7;18.9)	22.1 (18.9;25.8)	19.8 (16.9;23.1)	14.0 (11.2;17.2)	12.5 (10.0;15.3)	22.1 (17.7;27.1)	19.8 (15.8;24.2)

Table 4
Dose Rate Effectiveness Factor (DREF) from 4 solid cancer meta-analyses comparing low dose/low-dose-rate studies to the life span study[a].

Low dose/low-dose-rate Studies in the Comparison	DREF (95% CI)
Jacob et al. (2009) Main analysis of 7 mortality studies[b]	0.83 (90% CI 0.53; 1.96)
Shore et al. (2017) All 22 LD/LDR studies (19 mort + 3 inci)[c]	3.0 (1.9; 7.7)
Shore et al. (2017) All studies, except Mayak workers[c]	1.9 (1.0; 11)
Shore et al. (2017) All mortality studies, except Mayak workers[c]	0.9 (0.5; 2.5)
Shore et al. (2017) All studies, but including only the Mayak workers without potential plutonium exposure[c]	2.0 (1.2; 6.2)
Hoel (2018), analysis of 12 LD/LDR studies[d]	2.6 (1.6; 7.1)
Kocher et al. (2018)[e]	1.3 (90% CI 0.47; 3.6)

[a] These comparisons used statistical modeling to match the LSS to individual low dose/low-dose-rate studies on sex, mean age at initial exposure, mean final attained age and dose conversion factors.
[b] (Jacob et al., Occ. Env. Med (BMJ). 66, 789–96, 2009)
[c] (Shore et al., *Int J Radiat Biol*, 93:1064–78, 2017).
[d] (Hoel D, *Int J Radiat Biol*, 94:307–314, 2018).
[e] (Kocher et al. *Health Phys* 114:602–622, 2018).

Table B1
Results of fitting a linear model to *solid cancer relative incidence* to the atomic bomb data at attained age 60 years after exposure at age 41 years applying the EPICURE-AMFIT code to the atomic survivor data of dataset 2 with respect to organ averaged dose.

RBE	β^*	γ_e	γ_a	s
10	0.361	−0.202	−1.65	0.312
35	0.288	−0.186	−1.64	0.341
60	0.238	−0.176	−1.64	0.361
80	0.208	−0.170	−1.63	0.373
100	0.185	−0.165	−1.63	0.383
Sasaki	0.320	−0.194	−1.62	0.292

*ERR/Gy.

Table B2
Results of fitting a linear model to *solid cancer absolute incidence* to the atomic bomb data at attained age 60 years after exposure at age 41 years applying the EPICURE-AMFIT code to the atomic survivor data of dataset 2 with respect to organ averaged dose.

RBE	β^*	γ_e	γ_a	s
10	19.3	−0.298	2.34	0.232
35	15.5	−0.281	2.31	0.261
60	12.8	−0.270	2.29	0.281
80	11.2	−0.264	2.28	0.293
100	9.99	−0.259	2.27	0.303
Sasaki	17.1	−0.290	2.37	0.212

*EAR per 10,000 PY Gy.

Table B3
Results of fitting a linear-quadratic model to *leukemia relative incidence* to the atomic bomb data at attained age 60 years after exposure at age 41 years applying the EPICURE-AMFIT code to the atomic survivor data of dataset 3 with respect to organ averaged dose.

RBE	β^*	δ^{**}	γ_a	γ_e
10	2.39	1.33	−1.12	−0.791
35	2.76	0.413	−1.12	−0.797
60	2.74	0.122	−1.13	−0.797
80	2.62	0.0364	−1.13	−0.797
100	2.46	0.000117	−1.13	−0.797
Sasaki	1.64	1.15	−1.11	−0.793

*in Gy^{-1}.
**in Gy^{-2}.

level of the cancer induction risks for a lunar mission lies, for every scenario, below the risk limit of 6.1%. Consequently, a half year or even longer space missions to the Moon are possible without exposing the

Table B4
Results of fitting a linear-quadratic model to *leukemia absolute incidence* to the atomic bomb data at attained age 60 years after exposure at age 41 years applying the EPICURE-AMFIT code to the atomic survivor data of dataset 3 with respect to organ averaged dose.

RBE	β^*	$\delta^{\#}$	γ_e	γ_a	s
10	1.99	0.970	0.420	−1.45	−0.200
35	2.12	0.342	0.412	−1.40	−0.207
60	2.08	0.112	0.408	−1.38	−0.212
80	1.99	0.0440	0.406	−1.38	−0.214
100	1.88	0.0114	0.405	−1.37	−0.216
Sasaki	1.39	0.874	0.418	−1.44	−0.201

*in $(10{,}000\ PY\ Gy)^{-1}$,#in 10,000 $PY^{-1}\ Gy^{-2}$.

Table B5
Variances of the dose response fit parameters (e.g., the β in Eq.(1)) for relative and absolute incidence for solid cancer and leukemia at attained age 60 years after exposure at age 41 years applying the EPICURE-AMFIT code to the atomic survivor data of dataset 2 and 3.

	Solid cancer		Leukemia			
RBE	ERR β^*	EAR β^{**}	ERR β^*	ERR $\delta^{\#}$	EAR β^{**}	EAR $\delta^{\#\#}$
10	0.00242	6.76	0.967	0.273	0.462	0.172
35	0.00152	4.27	0.745	0.0721	0.312	0.0471
60	0.00103	2.92	0.569	0.0243	0.224	0.0159
80	0.000788	2.25	0.463	0.0117	0.178	0.00762
100	0.000622	1.78	0.380	0.00625	0.145	0.00404
Sasaki	0.00182	5.11	0.621	0.159	0.318	0.102

*in Gy^{-1}, ## in Gy^{-2},** in $(10{,}000\ PY\ Gy)^{-1}$,## in 10,000 $PY^{-1}\ Gy^{-2}$.

Table B6
Results of fitting a linear dose response model to *solid cancer incidence* to the atomic bomb data at attained age 70 years after exposure at age 30 years applying the EPICURE-AMFIT code to the atomic survivor data of dataset 1 with respect to weighted colon dose. Note: the results for ERR are from a re-fit of the model that is unadjusted for smoking from Table 5 of Grant et al. (2017) and the corresponding EAR model, not given by Grant et al. (2017), was published by Walsh et al. (2019b).

Risk	β	γ_a	γ_e	s
ERR	0.502	−1.57	−0.213	0.286
EAR	53.3*	2.35	−0.320	0.139

*in $(10{,}000\ PY\ Gy)^{-1}$.

astronauts to an intolerable risk considering radiation induced cancer induction. However, considering the effective doses for Mars missions, the risk limit of 6.1% is exceeded by far, for all risks calculated in this study for every scenario of risk models and EAR baseline scaling.

Table B7
Results of fitting a linear quadratic dose response model to *leukemia incidence* to the atomic bomb data at attained age 70 years after exposure at age 30 years applying the EPICURE-AMFIT code to the atomic survivor data for dataset 3 with respect to weighted RBM dose.

Risk	β	δ	γ_a	γ_e	s_{woman}	s_{man}
ERR	0.790	0.950	−1.09	−0.808		
EAR	1.06*	1.09**	−1.48	0.412	−0.421	0

*in $(10{,}000\ \mathrm{PY\ Gy})^{-1}$.
**in $10{,}000\ \mathrm{PY}^{-1}\ \mathrm{Gy}^{-2}$.

Table B8
Resulting covariance matrix for the *ERR* fit parameters from fitting a linear dose response model to *solid cancer incidence* to the atomic bomb data at attained age 70 years after exposure at age 30 years applying the EPICURE-AMFIT code to the atomic survivor data of dataset 1 with respect to weighted colon dose.

ERR cov	β^*	γ_a	γ_e	s
β^*	0.00191	0.00282	0.00105	−0.000275
γ_a	0.00282	0.0557	−0.00500	0.00163
γ_e	0.00105	−0.00500	0.00261	−0.000309
s	−0.000275	0.00163	−0.000309	0.00345

*in Gy^{-1}.

Table B9
Resulting covariance matrix for the *EAR* fit parameters from fitting a linear dose response model to *solid cancer incidence* to the atomic bomb data at attained age 70 years after exposure at age 30 years applying the EPICURE-AMFIT code to the atomic survivor data of dataset 1 with respect to weighted colon dose.

EAR cov	β^*	γ_a	γ_e	s
β^*	22.8	0.290	0.116	−0.113
γ_a	0.290	0.0440	−0.00465	−0.00236
γ_e	0.116	−0.00465	0.00259	−0.000132
s	−0.113	−0.00236	−0.000132	0.00387

*in $(10{,}000\ \mathrm{PY\ Gy})^{-1}$.

Table B10
Resulting covariance matrix for the *ERR* fit parameters from fitting a linear quadratic dose response model to *leukemia incidence* to the atomic bomb data at attained age 70 years after exposure at age 30 years applying the EPICURE-AMFIT code to the atomic survivor data of dataset 3 with respect to weighted RBM dose.

ERR cov	β^*	δ^{**}	γ_a	γ_e
β^*	0.218	−0.0555	0.00466	0.0287
δ^{**}	−0.0555	0.123	0.0396	0.0242
γ_a	0.00466	0.0396	0.197	−0.0555
γ_e	0.0287	0.0242	−0.0555	0.0671

*in Gy^{-1}.
**in Gy^{-2}.

4.6. Uncertainties

The epidemiological data from the A-bomb survivors LSS are associated with large errors. In this study the uncertainties of the LSS fit parameters from the different excess risk models are included using Monte Carlo simulations. Nevertheless, there are additional uncertainties which can have an impact on the risk calculations. An example of this is the fixed neutron RBE of 10 or the use of survival curves in the cancer risk calculation. Additionally, it has to be noted that the A-bomb survivors were exposed to γ-rays and neutrons. The models used to calculate the cancer risk in this study are based on these

Table B11
Resulting covariance matrix for the *EAR* fit parameters from fitting a linear quadratic dose response model to *leukemia incidence* to the atomic bomb data at attained age 70 years after exposure at age 30 years applying the EPICURE-AMFIT code to the atomic survivor data of dataset 3 with respect to weighted RBM dose. For males the column and row with the gender parameter s can be neglected.

EAR cov	β^*	δ^{**}	γ_a	γ_e	s
β^*	0.302	−0.0746	0.0820	−0.0204	−0.0393
δ^{**}	−0.0746	0.175	0.0545	−0.0114	−0.0273
γ_a	0.0821	0.0545	0.112	−0.0288	−0.00620
γ_e	−0.0204	−0.0114	−0.0288	0.0116	0.00162
s	−0.0393	−0.0273	−0.00620	0.00162	0.0551

*in $(10{,}000\ \mathrm{PY\ Gy})^{-1}$.
**in $10{,}000\ \mathrm{PY}^{-1}\ \mathrm{Gy}^{-2}$.

epidemiological data, but astronauts are mainly exposed to protons and heavy ions (GCR). The uncertain biological effectiveness of these particles and the different dose-rate of the GCR lead to additional uncertainties, which must be accounted for in future work by applying a detailed dosimetric model to obtain the actual organ doses that are required for the risk analysis presented here.

5. Conclusion

The risk assessment methods LAR and REIC can both be applied to calculate space radiation induced cancer incidence risks based on models fitted to the most recent epidemiological data of A-bomb survivors. Nevertheless, one has to be aware that both methods are based on uncertain quantities such as survival curves and that REIC includes deterministic radiation induced non-cancer mortality risks, modelled based on the data of the general population, which may lead to an underestimation of the risks for astronauts. Additionally, a neutron RBE higher than 10 has a large impact on LAR and REIC and reduces the risk up to almost 50%. Including an EAR baseline scaling also increases the risks by 0.4%–8.1% for the space missions considered here, but further work is required in order to fully evaluate the advantages and disadvantages of applying this type of scaling. Using an EAR model instead of an equally weighted excess risk model can decrease the risks by 0.4%–4.1% if no EAR baseline scaling is applied. If EAR baseline scaling is included, the calculated risks with the EAR- and the equally weighted model, as well as the risks calculated with the ERR model are almost identical and only small differences in their uncertainties are visible.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A

ERR and EAR risk models based on dataset 2 and 3

The ERR and EAR models applied to calculate REIC and LAR based on dataset 2 have the same structure as the models in Eq. (1), but the calculations are centered around an exposed age e of 41 years and an attained age a of 60 years. Therefore, different modifying functions are used. For solid cancer:

$$\mu_s(e, a, s) = \exp\left(\gamma_e\left(\frac{e-41}{10}\right) + \gamma_a \log\left(\frac{a}{60}\right)\right)(1 \mp s) \tag{A1}$$

where - is used for males and + for females. The fit parameters γ_e, γ_a and s are gender-averaged. For leukemia dataset 3 and the models from Eqs. (3) to (4) are used and with the different centring the corresponding modifying functions are:

$$\mu_{L1}(e, a) = \exp\left(\gamma_e log\left(\frac{a-e}{19}\right) + \gamma_a \log\left(\frac{a}{60}\right)\right) \tag{A2}$$

$$\mu_{L2}(e, a, s) = \exp\left(\gamma_e\left(\frac{e-41}{10}\right) + \gamma_a \log\left(\frac{a}{60}\right)\right)*\exp(s) \tag{A3}$$

The fit parameters γ_e and γ_a are gender-averaged while s is only given for women and set to 0 for men.

Appendix B

Here the fit parameters and the corresponding covariance matrices resulting from fitting different models to data of the LSS for different neutron RBEs are shown.

Appendix C

Here the analogue figures to Figs. 2–4 for women are shown.

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